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Greener Synthesis, Antimicrobial, Antioxidant and Insect Antifeedant Activities of some 2-(9-anthryl)-3-(substituted phenyl)bicyclo [2.2.1]hept-5-ene-2-yl ketones

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Abstract:A series containing nine of 2-(9-anthryl)-3-(substituted phenyl)bicyclo [2.2.1]hept-5-ene-2-yl methanones were synthesized by fly-ash catalyzed aqueous phase Diels-Alder [4+2] cycloaddition of reaction of substituted styryl 9-anthryl ketones and cyclopentadiene. The yields of the ketones were more than 65%. The synthesized ketones were characterized by their physical constants, micro analysis and spectral data. The effect of solvent on the cycloaddition reaction was studied. The antibacterial and antifungal activities of these ketones were evaluated against their strains using Bauer-Kirby method. The antioxidant activities of these methanones were studied using DPPH radical scavenging method. The insect antifeedant activities of these ketones were studied by castor leaf disc bio-assay of 4th instar larvae *Achoea Janata L* method.

Keywords:9-Anthryl chalcones, Methanones, Greener synthesis, IR and NMR spectra,Pharmacological effects, Insect antifeedant activity

1 Introduction

Currently, researchers and organic chemists paid more attention to the Diels-Alder reaction for stereo selective synthesis of six-membered bicyclic compounds by [4+2] cycloaddition of a diene and dienophiles[1]. Whether this reaction is reversible in thermal condition or not it is called as retro-Diels-Alder reaction. The reactivity, selectivity, *endo-*, *exo-* mechanistic aspects and solvent effects of this Diels-Alder reaction has been reported [2-6]. Presently, aqueous phase Diels-Alder reaction is important for the synthesis of organic substrates especially bicyclo compounds with stereo selectivity, specificity, due to easy handling technical procedure, non-hazardousness, non-polluting to the environment and good yields[1,7,8].

Reidant and Breslow [9] have studied the aqueous phase reaction of cyclopentadiene and vinyl methyl ketones in water and the reaction rate is greater than 700 times faster than in organic solvents. Many catalysts including Lewis acids4,Bronsted acids[4,10], Asymmetric catalyst with helical polymers[11], Cu^{2+} ion-mediated nanotubes[12], DNA and Micellar based catalysts[7, 13, 14, 15, 16] have been employed for this [4+2] cycloaddition Diels-Alder reaction of cyclopentadiene(diene) and *E*-chalcones(dienophiles). The vinyl ketones, aza- vinyl ketones, bicyclo methanones possess antimicrobial activities [17]. The hydroxylated and methoxylated organic compounds possess antioxidant activities [18, 19, 20]. The halo substituted enones possess insect antifeedant activities[19,20, 21, 22, 23]. The waste air-pollutant fly-ash has many chemical compounds such as [18, 19, 2324]SiO_2, Fe_2O_3, Al_2O_3, CaO, MgO, organic mud and insoluble residues. The waste fly-ash is used as catalyst for organic synthesis. The fly-ash particles are in the silt-sized range of 2-50 microns [25]. Glass, mullite-quartz, and magnetic spinel are the three major mineralogical matrices identified in fly ash. The elements Si, Al, Fe, Ca, C, Mg, K, Na, S, Ti, P, and Mn are constituents of fly ash. The solubility of fly ash has been extensively investigated and is largely dependent on factors specific to the extraction procedure. Review of literature reveals that long-term leaching studies predict that fly ash will lose substantial amounts of soluble salts over time, but simulation models predict that the loss of trace elements from fly ash deposits through leaching will be very slow.

Small amounts of radioisotopes are found to be the constituents of fly ash which do not appear to be hazardous. Recent literature review noticed for the synthesis of some aryl heptene [2.2.1] methanones [26-31] that there are some Within the aforementioned view, there is no report available for the synthesis of 9-anthryl based heptane [2.2.1] methanones by aqueous phase fly-ash catalyzed Diels-Alder reaction of cyclopentadiene and 9-anthryl chalcones. Hence, the author has made efforts to synthesize some 9-anthryl based heptene [2.2.1] methanones and evaluated their pharmacological activities such as antimicrobial, antioxidant and insect antifeedant

activities using the respective antimicrobial strains with Bauer-Kirby[32], DPPH radical scavenging[33] and Dethler's[34] disc-diffusion bio-assay method.

2 Material and Methods

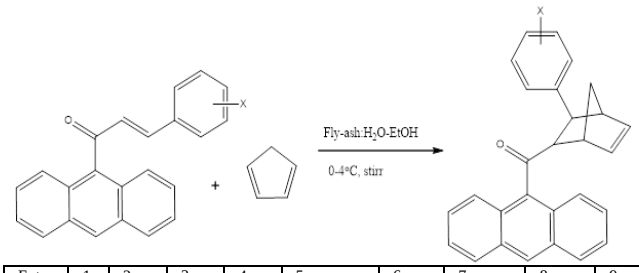
2.1 General

All chemicals were procured from Sigma-Aldrich and E-Merck brands. Fly ash was collected from Thermal Power Plant-II, Neyveli Lignite Corporation (NLC), Neyveli, Tamil Nadu, India. Melting points of all bicyclo[2.2.1]hepene-2-yl methanones were determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000-400 cm^{-1}) were recorded on Thermo scientific Nicolet iS5, US made Fourier transform spectrophotometer. The NMR spectra of selective compounds were recorded in Bruker AV 400 spectrometer operating at 400 MHz for ^{1}H NMR spectra and 100 MHz for ^{13}C NMR spectra in $CDCl_3$ solvent using TMS as internal standard. Electron impact and chemical ionization mode FAB^{+} mass spectra were recorded with a SHIMADZU spectrometer.

2.2 Synthesis of 9-antrhyl chalcones

The substituted styryl-9-anthryl ketones were synthesized by literature method [35].

2.3 General procedure for synthesis of 2-(9-anthryl)-3-(substituted phenyl)bicyclo [2.2.1]hept-5-ene-2-yl ketones



Entry	1	2	3	4	5	6	7	8	9
X	H	3-Br	3-Cl	4-Cl	4-N$(CH_3)_2$	4-OH	4-OCH_3	4-CH_3	4-NO_2

Scheme 1. Synthesis of 2-(9-anthryl)-3-(substituted phenyl)bicyclo [2.2.1]hept-5-ene-2-yl ketones by an aqueous phase fly-ash catalyzed Diels-Alder reaction of 9-anthryl chalcones and cyclopentadiene.

Appropriate equi-molar quantities of 9-anthyl chalcones (2 mmol) in 15 mL of ethanol, cyclopentadiene (2 mmol), and 1g of fly-ash in 20 mL of water were stirred for 6 h in 0-4°C **(Scheme 1)** and the reaction mixture was kept overnight. The completion of the reaction was monitored by a thin layer chromatogram. Dichloromethane (10 mL) was added and the extract was separated by filtration. The filtrate was washed with water, brine (10 mL), dried over on anhydrous Na_2SO_4 and concentrated gave the solid product. The crude product was further purified by recrystallization with ethanol.

2.4 Measurement of anti-microbial activities

The antimicrobial activities of prepared bicycle-[2.2.1]heptene-2-ylmethanones have been evaluated by measuring the mm of zone of inhibition of the compounds against the bacterial and fungal strains. In the present study the author has chosen two gram positive pathogenic strains of *Staphylococcus aureus*, *Entrocccusfaecalis* while *Escherichia coli*, *Klebsiella species*, *Psuedomonas* and *Proteus vulgaris* were the gram negative strains. The disc diffusion technique is followed using the Kirby-Bauer [32] method, at a concentration of 250µg/mL with Ampicillin and Streptomycin taken as the standard drugs. For the study of antifungal activities of all methanones using *Candida albicans* as the fungal strain, the disc diffusion technique was followed for the antifungal activity whereas the dilution method [32] used for the two other strains *Penicillium*species and *Aspergillusniger*. The drugs dilution was 50µg/mL. *Grisseofulvin* was taken as the standard drug.

2.4.1 Measurement of antibacterial activities

Antibacterial sensitivity assay was performed using Kirby-Bauer [32] disc diffusion technique. In each Petri plate approximately 0.5 ml of the test bacterial sample was spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs of 5mm diameter made up of Whatmann No.1 filter paper, impregnated with the solution of the compound were placed on the medium using sterile forceps. The plates were incubated for 24 hours at 37°C by keeping the plates upside down to prevent collection of water droplets over the medium. After 24 hours, the plates were visually examined and the diameter values of the zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.

2.4.2 Measurement of Antifungal sensitivity assay

Antifungal sensitivity assay was performed using Kirby-Bauer [32] disc diffusion technique. PDA medium was prepared and sterilized as aforementioned. It was poured (ear bearing heating condition) in the Petri-plate which was already filled with 1 mL of the fungal species. The plate was rotated clockwise and counter clock-wise to spread the species uniformly. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15mg of the methanone in 1mL of DMSO solvent. The medium was allowed to solidify and kept for 24 h. Then the plates were visually examined and the diameter values of zone of inhibition were measured. Triplicate results were

recorded by repeating the same procedure.

2.5 Antioxidant activity

The antioxidant activities of all synthesized methanones have been evaluated by the DPPH radical scavenging effect[25,33]. The 0.1M acetate was prepared by dissolving 1.64 g of sodium acetate in 15 mL of water and 150 µL of acetic acid. The final volume was adjusted to 20 mL by adding water. The 0.2 mmol of DPPH solution was prepared by dissolving 3.9 g of DPPH in 50 mL of ethanol. α-Tocofereol (1mg in 10 mL of ethanol) solution was prepared. A series of test tubes were arranged with 1.0 mL of buffer solution mixed with 0.5 mL of DPPH solution.

A series of various concentrations of synthesized methanones and α-Tocofereol (1µg in 1 ml of ethanol) was added to each tube and mixed well. After 30 minutes in room temperature the absorbance of each solution was measured by UV spectrophotometer at 517 nm. A mixture of buffer solution and ethanol was used as the reference for the spectrophotometer. A graph was plotted with the weight of the compound versus absorptions and IC_{50} values were determined. The antioxidant activity was expressed in terms of IC50 (µg/mL, concentration required to inhibit DPPH radical formation by 50%). α-Tocofereol was used as a positive control. The radical scavenging activity was calculated as,

$$\text{DPPH radical scavenging activity (\% of inhibition)} = \frac{\text{Control absorbance - Sample absorbance}}{\text{Control absorbance}} \times 100$$

2.6 Measurement of Insect Antifeedant activity

Generally organic compounds which possess carbonyl, unsaturation and halogen substitutions, possess insect antifeedant activity [21,22]. Therefore, the author wished to examine the insect antifeedant activity of these bicyclo[2.2.1]heptene-2-yl methanone derivatives and found them to be active as insect antifeedants. This test was performed with a 4th instar larva *Achoeajanata* L against castor *semilooper*,that was reared as described on the leaves of castor, *Ricinuscommunis* in the laboratory at the temperature range of 26°C ±1°C and a relative humidity of 75-85%. The leaf – disc bioassay methodwas used against the 4th instar larvae to measure the antifeedant activity. The 4th instar larvae was selected for testing because the larvae at this stage feed very voraciously.

Castor leaf discs of 1.85 cm diameter were punched and intact with the petioles. The synthesized aryl bicyclo [2.2.1] heptene-2-yl methanones were dissolved in acetone at a concentration of 200 ppm dipped for 5 minutes. The leaf discs were air-dried and placed in one litre beaker containing little water in order to facilitate translocation of water. Therefore, the leaf discs remained fresh throughout the duration of the rest, 4th instar larvae of the test insect, which had been preserved on the leaf discs of all bicyclo[2.2.1]heptene-2-yl methanones and allowed to feed on them for 24 h. The area of the leaf discs consumed was measured by Dethler'smethod[34].

3 Results and Discussion

Attempts have been made for the synthesis of aryl bicyclo[2.2.1]hepten-2-yl methanone derivatives by aqueous phase fly-ash catalyzed Diels-Alder reaction with cyclopentadiene as diene and *E*-chalcones as dienophiles. Hence, the author has synthesized aryl bicyclo [2.2.1] heptane-2-yl-methanones by aqueous phase Diels-Alder reaction of *E*-enones and cyclopentadiene under solvent-free cooling condition. During the reaction the chemical species present in the fly-ash catalyzed the [4+2] cycloaddition reaction. In this reaction the obtained yield was more than 60%. The analytical physical constants and micro analysis data are presented in **Table 1.**

The reusability of catalyst in this cycloaddition reaction was studied with 2 mmol of 9-anthryl chalcone and 2 mmol of cyclopentadiene (**entry 1**) and is presented in **Table 2**.

Table 1. The physical constants and mass fragments of aryl bicyclo[2.2.1]heptene-2-yl-methanone derivatives.

Compd.	X	MW	Mp(°C)	Yield (%)	Micro analysis (%)		
					C	H	N
1	H	374	116-117	65	(89.81)	(5.25)	---
2	3-Br	452	104-105	63	(74.18)	(4.67)	---
3	3-Cl	408	99-100	60	(82.24)	(5.18)	---
4	4-Cl	408	84-85	62	(82.24)	(5.18)	---
5	4-NMe_2	418	112-113	63	(86.30)	(6.52)	(3.35)
6	4-OH	390	107-108	62	(86.13)	(5.68)	---
7	4-OMe	404	113-114	65	(86.11)	(5.98)	---
8	4-Me	388	127-128	64	(89.66)	(6.23)	---
9	4-NO_2	419	121-122	60	(80.17)	(5.05)	(3.34)

Table 2.The effect of reuse of the catalyst on the yield of the aqueous phase Diels-Alder reaction of styryl 9-anthyl ketone and cyclopentadiene (compound **1**).

Run	**1**	**2**	**3**	**4**	**5**
Yield %)	65	60	53	40	40

The first run gave 65% of the product. The second and third runs gave 60 and 53% respectively. The fourth and fifth runs gave 40%. The chalcone containing electron donating substituents (OCH_3) gave higher yield than electron withdrawing (halogens and nitro) substituents. The effect of catalyst on this reaction was studied by varying the catalyst quantity from 0.1 to 0.4g. As the catalyst quantity increased from 0.1 to 0.4 g the percentage of product increased from 60-65%. With further increase in the catalyst amount of more than 0.4 g, there was no increase in the percentage of the product. The effect of catalyst loading is shown in **Fig.1**.

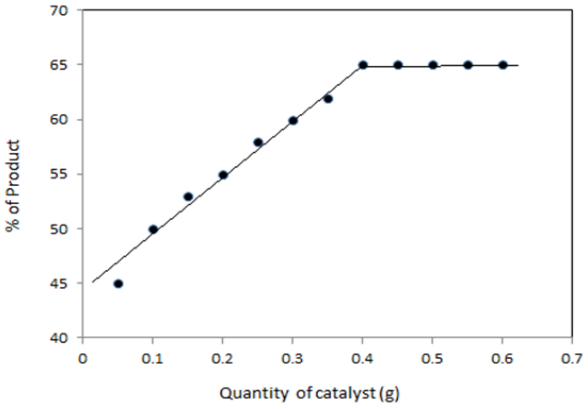


Figure 1. The effect of catalyst loading.

The optimum quantity of catalyst loading for the reaction was found to be 0.4 g. The effect of solvents on this reaction (**entry 1**) was studied with the same quantity of reactants with methanol, dichloromethane, dioxane and tetrahydrofuran and is presented in **Table 3**. The higher yield was obtained in ethanol with fly-ash in water as the medium. The infrared and NMR data of all compounds are summarized as follows.

Table 3. The effect of solvents on the aqueous phase Diels-Alder reaction of styryl 9-anthryl ketone and cyclopentadiene (compound**1**).

Solvent	**Ethanol**	**Methanol**	**Dichloromethane**	**Dioxane**	**Tetrahydrofuran**
Yield (%)	65	63	62	60	62

1. (Anthracene-9-yl)(3-phenylbicyclo[2.2.1]hept-5-en-2-yl)methanone: IR(KBr, 400-4000cm^{-1}) ν= 2995, 2854, 1648, 1563, 1326, 1287, 1065, 956, 684; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.708(2H, dd, $H_{1,4}$, J=8 and 4Hz), 3.487 (1H, t, H_2, J =19Hz), 3.536 (1H, t, H_3, J=19Hz), 6.172(1H, d, $H_{5,6}$, J=16Hz), 1.829(1H, dd, H_7, J=6 and 4 Hz), 1.685(1H, dd, $H_{7'}$, J=6.4 and 5.6Hz), 7.214-8.456 (14H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 198.35(CO), 46.73($C_{1,4}$), 55.37(C_2), 45.31(C_3), 136.72($C_{5,6}$), 46.32(C_7), 125.82-146.71 (Ar-C); Mass (m/z): 374[M^+], 297, 205, 177, 110, 101, 92, 91, 77, 28,15.

2.(3-(3-Bromophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone:IR(KBr,400-4000 cm^{-1}) ν= 2936, 2852, 1654, 1565, 1314, 1247, 1014, 925, 621; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.804(2H, dd, $H_{1,4}$, J=8 and 8.8Hz), 3.573 (1H, t, H_2, J =19Hz), 3.371 (1H, t, H_3, J=19Hz), 6.172(1H, d, $H_{5,6}$, J=16Hz), 1.749(1H, dd, H_7, J=9.6 and 4 Hz), 1.653(1H, dd, $H_{7'}$, J=4 and 5.2Hz), 7.241-8.413 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 201.7(CO), 47.37($C_{1,4}$), 52.07(C_2), 44.97(C_3), 136.72($C_{5,6}$), 135.62(C_6), 47.01(C_7), 122.72-148.25(Ar-C); Mass (m/z): 452[M^+], 453[M^{2+}]373, 297, 205, 196, 177, 168, 97, 91, 79, 76, 28.

3. (3-(3-Chlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone: IR(KBr, 400-4000cm^{-1}) ν= 2995, 2896, 1658, 1532, 1467, 1358, 1028, 958, 687, 421; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.701(2H, dd, $H_{1,4}$, J=6.8 and 4.8Hz), 3.542 (1H, t, H_2, J =19Hz), 3.435(1H, t, H_3, J=19Hz), 6.852(1H, d, $H_{5,6}$, J=16Hz), 1.832(1H, dd, H_7, J=7.6 and 4.8 Hz), 1.714(1H, dd, $H_{7'}$, J=4.8 and 4 Hz), 7.185-8.425 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 200.91(CO), 41.97($C_{1,4}$), 52.08(C_2), 45.74(C_3), 136.81($C_{5,6}$), 134.21(C_6), 47.14(C_7), 123.324-147.78(Ar-C); Mass (m/z): 408[M^+], 410[M^{2+}], 373, 297, 205, 177, 92, 91, 77, 35, 26.

4. (3-(4-Chlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone: IR(KBr, 400-4000cm^{-1}) ν= 3012, 2965, 2842, 1659, 1534, 1257, 1039, 854, 628; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 2.977(2H, dd, $H_{1,4}$, J=8 and 6.4Hz), 3.564 (1H, t, H_2, J =19Hz), 3.521(1H, t, H_3, J=19Hz), 6.747(1H, d, $H_{5,6}$, J=16Hz), 1.822(1H, dd, H_7, J=5.6 and 6.4 Hz), 1.615(1H, dd, $H_{7'}$, J=7.6 and 5.6 Hz), 7.125-8.453 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 201.06(CO), 47.23($C_{1,4}$), 52.06(C_2), 45.23(C_3), 136.22($C_{5,6}$), 134.26(C_6), 45.19(C_7), 125.841-149.325(Ar-C); Mass (m/z): 408[M^+], 410[M^{2+}], 382, 373, 359, 347, 297, 205, 177, 92, 91, 77, 66, 35, 28, 26, 14.

5. (3-(4-Dimethylaminophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl) methanone: IR(KBr, 400-4000cm^{-1}) ν= 3365, 2996, 2854, 1635, 1587, 1468, 1235, 1027, 954, 684; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.853(2H, dd, $H_{1,4}$, J=4 and 5.2 Hz), 3.497 (1H, t, H_2, J =19Hz), 3.387(1H, t, H_3, J=19Hz), 6.173(1H, d, $H_{5,6}$,J=16Hz), 1.804(1H, dd, H_7, J=6 and 8 Hz), 1.716(1H, dd, $H_{7'}$, J=6.4 and 5.2 Hz), 3.654(3H, s, CH_3), 6.681-8.542 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 201.93(CO), 46.92($C_{1,4}$), 52.07(C_2), 45.17(C_3), 137.74($C_{5,6}$), 136.58(C_6), 46.23(C_7), 45.36(CH_3), 112.52-148.52(Ar-C);Mass (m/z): 418[M^+], 402,387, 373, 297,

205, 177, 120, 92, 91, 77, 44, 30, 28, 15.

6. (3-(4-Hydroxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl) methanone: IR(KBr, 400-4000cm^{-1}) ν= 3498, 29984, 2854, 1682, 1532, 1402, 1028, 652, 421; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.995(2H, dd, $H_{1,4}$, J=5.2 and 7.6 Hz), 3.472 (1H, t, H_2, J =19Hz), 3.372(1H, t, H_3, J=19Hz), 6.831(1H, d, $H_{5,6}$, J=16Hz), 1.812(1H, dd, H_7, J=8 and 5.2 Hz), 1.614(1H, dd, $H_{7'}$, J=4.8 and 7.6 Hz), 6.714 (1H, s OH), 6.672-8.437 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 199.77(CO), 47.24($C_{1,4}$), 52.73(C_2), 45.76(C_3), 136.72(C_5), 134.11(C_6), 47.14(C_7), 115.521-138.627(Ar-C);Mass (m/z): 390[M$^+$], 373, 297, 213, 205, 185, 187, 177, 94, 93, 91, 26, 28, 17.

7. (3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone: IR(KBr, 400-4000cm^{-1}) ν= 2996, 2885, 1638, 1596, 1435, 1025, 964, 821, 628, 428; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.708(2H, dd, $H_{1,4}$, J=5.6 and 8 Hz), 3.493 (1H, t, H_2, J =19Hz), 3.401(1H, t, H_3, J=19Hz), 6.173(1H, d, $H_{5,6}$, J=16Hz), 1.817(1H, dd, H_7, J=8 and 5.2 Hz), 1.624(1H, dd, $H_{7'}$, J=4.8 and 7.2 Hz), 4.031 (1H, s OCH_3), 6.912-8.452 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 198.37(CO), 46.92($C_{1,4}$), 51.73(C_2), 44.84(C_3), 136.17(C_5), 134.21(C_6), 46.73(C_7), 59.63(OCH_3), 113.965-138.854(Ar-C);Mass (m/z): 404[M$^+$], 389, 373, 205, 177, 107, 92, 91, 77, 31, 28, 26, 15.

8. (3-(4-Methylphenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone: IR(KBr, 400-4000cm^{-1}) ν= 2968, 2903, 2885, 1638, 1598, 1235, 1087, 835, 628; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 3.830(2H, dd, $H_{1,4}$, J=8 and 5.6 Hz), 3.573 (1H, t, H_2, J =19Hz), 3.491(1H, t, H_3, J=19Hz), 6.217(1H, d, $H_{5,6}$, J=16Hz), 1.885(1H, dd, H_7, J=6 and 7.6 Hz), 1.626(1H, dd, $H_{7'}$, J=4.8 and 6 Hz), 2.91 (1H, s, CH_3), 7.115-8.453 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 194.76(CO), 46.92($C_{1,4}$), 51.84(C_2), 44.69(C_3), 137.44(C_5), 134.68(C_6), 46.12(C_7), 24.75(CH_3), 124.321-143.854(Ar-C); Mass (m/z): 388[M$^+$], 373, 297, 211, 205, 185, 183, 177, 107, 92, 91,77, 26, 15,

9. (3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl) methanone:IR(KBr, 400-4000cm^{-1}) ν= 3268, 2996, 2804, 1658, 1534, 1497, 1204, 1085, 962, 810, 654, 429; ^{1}H NMR(400MHz, $CDCl_3$, 25°C, TMS) δ= 4.005(2H, dd, $H_{1,4}$, J=6 and 4 Hz), 3.603 (1H, t, H_2, J =19Hz), 3.473(1H, t, H_3, J=19Hz), 6.712(1H, d, $H_{5,6}$, J=16Hz), 1.950(1H, dd, H_7, J=8 and 4 Hz), 1.668(1H, dd, $H_{7'}$, J=4.8 and 8 Hz), 7.415-8.452 (13H, m, Ar-H); ^{13}C NMR(100MHz, $CDCl_3$, 25°C, TMS) δ= 197.92(CO), 46.72($C_{1,4}$), 52.01(C_2), 45.73(C_3), 137.92C_5), 135.72(C_6), 46.14(C_7), 123.514-145.257(Ar-C); Mass (m/z): 419[M$^+$], 373, 297, 242, 216, 214, 205, 177, 122, 102, 77, 46, 26.

3.1 Antibacterial sensitivity assay

The disc-diffusion technique was followed using the Bauer-Kirby [32] method, at a concentration of 250 μg/mL, with ampicillin and streptomycin being used as the standard drugs. The measured antibacterial activities of all methanones are presented in Table 4. Compounds **1-4**showed the maximum zone of inhibition against *Escherichia coli*, at 20–24 mm, compared to other methanones such as **5** and **7**.These latter compoundswere moderately active, with 13–19 mm zones of inhibition. Ketone **6**was active with an 8–12 mm of zone of inhibition. The parent compounds **1, 8**and **9**were inactive. The methanones **2-4** were found to be effective against *S. aureus* strain with 20–24 mm of zones of inhibition. Compounds **5-7** were moderately active with 13–19 mm of zones of inhibition. Ketones **6 and 7** were moderately active with an 8–12 mm zone of inhibition.

Compound **1** was inactive against *S. aureus*. The methanone derivatives **2 - 4**were shown to be more active against *Pseudomonas* with more than 20 mm zone of inhibition, whereas the other derivatives showed between 12–19 mm zones of inhibition. Compounds **1** and **9** were inactive against the *Pseudomonas aeruginosa* strain. Ketones**2-4**were more effective against the *Klebsiellapneumoniae* strain with 20–24 mm zones of inhibition, whereas ketones **5** and **6** showed moderate activity with a 13–19 mm zone of inhibition. Methanone **7** was active with an 8–12 mm zone of inhibition. Ketones **1** and **9** were inactive against the *K. pneumoniae* species. The methanone derivatives **2-4** were active when they were screened with *Phaseolus vulgaris* with 20–24 mm zones of inhibitionand compound **17** was moderately active with 13–19 mm zones of inhibition. Methanones **1, 8** and9 were ineffective against the *P. vulgaris* strain. Ketones **2-4** showed greater activity against *Enterococcus faecalis*, with 20–24 mm zones of inhibition. Compounds **7** and **8** were moderately active with 13–19 mm zones of inhibition. Methanones **5** and **6** were active with 8–12 mm zones of inhibition. The ketones **1** and **9** were inactive when they were screened against *E. faecalis.*

3.2 Antifungal sensitivity assay

The observed antifungal activities of all prepared methanones are presented in Table 4**.** The study of antifungal activities of all methanones against *C. albicans*, showed that the three compounds **5, 8** and **9** were effective with 20 mm as the zone of inhibition in 250 μg/ disc whereas methanones **16** and **17** were active with 13-19 mm zone of inhibition and compounds **3** and **4** were the least active with 8-12 mm zone of inhibitions. Compounds **5, 8** and **9** were visible against *Penicillium* species, in the development of the least fungal colony and 2-3

Table 4. Antibacterial[a], antifungal[b] and antioxidant[c] activities of (9-anthryl)-3-(substitutedphenylbicyclo [2.2.1]hept-5-en-2-yl)methanones.

Cpd.	Antibacterial activity						Antifungal activity			Antioxidant activity (DPPH radical scavenging)
	E. coli	*S. aures*	*P. aeruginosa*	*K. pneumoniae*	*P. vulgaris*	*E. faecalis*	*C. albicans*	*Penicilliumsp.*	*A. niger*	
1	–	–	–	–	–	–	–	–	–	18.78±1.18
2	++	++	++	++	++	++	–	–	+	13.81±1.94
3	++	++	++	++	++	++	±	+	+	19.58±1.09
4	++	++	++	++	++	++	±	±	±	22.95±1.54
5	±	+	+	+	+	+	++	+	++	21.45±1.64
6	+	±	±	+	+	±	+	+	–	37.95±1.24
7	±	+	±	±	±	±	+	±	–	35.01±1.65
8	–	±	+	–	–	+	++	++	++	21.34±1.72
9	–	–	–	–	–	–	++	++	++	11.04±1.82

[a]Disc size: 6.35 mm; duration: 24-45 h; standard: ampicillin (30–33 mm) and streptomycin (20–25 mm); control: methanol; –: no activity;
±: active (8–12 mm); +: moderately active (13–19 mm); ++: active (20–24 mm).
[b]Standard: griseofulvin and gentamycin; duration: 72 h; control: methanol; medium: Potato dextrose agar; ++: no fungal colony; +: one fungal colony; ±: two-three fungal colonies; –: Multiple fungal colonies.
[c]Standard: α-Tocopherol (39.14±1.57).

colonies were recorded for the compounds **3** and **6**. The inhibition of ketones against *A.niger* was less fungal colonies in three compounds **5, 8** and **9** being highly active followed by **2-4**. Presence of a chloro, dimethylamino, methoxy, and nitro substituents is responsible for antimicrobial activities of methanones.

3.3 Antioxidant activity

The antioxidant activities of the 9-anthryl based methanones were measured using DPPH radical scavenging method. The observed antioxidant activities of methanones are presented in Table 4. Table 4, shows the hydroxyl and methoxy substituted methanones (**6** and **7**) with significant antioxidant activity.

3.4 Insect antifeedant activity

The observed antifeedant activity of bicyclo[2.2.1]hepane-2-yl methanones was presented in **Table 5**, which reveals that compound **4** (3-(4-dichlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanone was found to reflect satisfactory antifeedant. This test is performed with insects which ate only two-leaf disc soaked under the solution of this compound. Compound **3** showed enough antifeedant activity but less than compound **4**. Further compound **4** was subjected to measure the antifeedant activity at different concentrations (50, 100, 150 ppm) and the observation reveals that as the concentrations decreased, the activity also decreased. It is observed from the results in **Table 6** and compound **4** (3-(2,4-dichlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)methanoneshowed an appreciable antifeedant activity at 150 ppm concentration.

Table 5. The insect antifeedant activities of (9-anthryl)-3-(substituted phenyl)-bicyclo[2.2.1]hept-5-en-2-yl methanones

Cpd.	4-6 pm	6-8 pm	8-10 pm	10-12 pm	12-6 pm	6-8 pm	8 am-12 Nn	12 Nn-2 pm	2-4 pm	Total leaf disc consumed in 24 h
1	1	0.5	1	0.5	0.5	1	0.5	1	1	7
2	0.5	0.25	0.25	0.5	0.5	0.5	1	0	0.5	4
3	0.25	0	0	0.25	0.5	0.5	0.5	1	0.5	3.5
4	0.25	0	0.25	0.25	0.25	0.5	0.5	0.5	0.5	3
5	1	2	2	1	0	0	1	1	1	9
6	1	1	1	0.5	0.5	1	1	1	1	8
7	1	0.5	1	1	1	0.5	1	0.5	0.5	7
8	1	0.5	1	1	1	1	0.5	0.5	0.5	7
9	1	1	0.5	0.5	1	1	1	1	1	8

Number of leaf discs consumed by the insect (Values are mean + SE of five).

Table 6. Antifeedant activity of compound **4** (3-(4-chlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl) methanoneshowed an appreciable antifeedant activity at 3 different concentrations

ppm	4-6 pm	6-8 pm	8-10 pm	10-12 pm	12-6 pm	6-8 pm	8 am-12 Nn	12 Nn-2 pm	2-4 pm	Total leaf disc consumed in 24 h
50	0.25	0.25	0.25	0	0	0	0	0	0	0.75
100	0.5	0.25	0.25	0	0	0	0	0	0	1
150	0.25	0.25	0	0	0	0	0	0	0	0.5

Number of leaf discs consumed by the insect (Values are mean + SE of five).

4 Conclusions

A series of 2-(9-anthryl)-3-(substituted phenyl)-bicyclo[2.2.1]hept-5-en-2-yl methanone derivatives have been synthesized by aqueous phase fly-ash catalyzed Diels-Alder [4+2] cycloaddition of cyclopentadiene and aryl *E*-9-anthryl chalcones. The yields of the methanones are more than 60%. The antimicrobial activities of the methanones have been evaluated using Bauer-Kirby methods. Methanone derivatives containing halogens, dimethylamino, methoxy, and nitrosubstituents have shown antimicrobial activities. The antioxidant activities of the methanones were measured by DPPH radical scavenging method. The compounds containing hydroxyl and methoxy substituents showed antioxidant activity. The insect antifeedant activities of methanones have been evaluated using Dethler'sleaf-disc bioassay method. Methanone **4**(3-(4-chlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(9-anthryl)-methanone showed an appreciable antifeedant activity.

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